K-M graphs. **CONCLUSIONS:** Due to very limited availability of trials with robust endpoints and long-term follow-up, alternative options for establishing comparative efficacy must be used for decision making in relapsed or refractory MCL. These alternatives include implementing comparisons of single-arm trial data without adjustment (i.e., via naïve comparison) or methods such as match-adjusted indirect comparison (MAIC) to derive comparative estimates. MAIC is a relatively novel method and may be difficult to implement given the heterogeneity in trial designs and patient-level characteristics in MCL trials. The scarcity of K-M data to inform PFS and OS of certain comparators further limits the comparisons that can be made through modeling.

PCN11

THE EFFICACY OF CURRENT TREATMENT OPTIONS FOR METASTATIC CERVICAL CANCER

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OBJECTIVES: The prognosis of patients with metastatic cervical cancer (CC) remains poor, and treatment options are limited, with no single agent or combination of agents recognised as standard of care; cisplatin/paclitaxel is the therapy most cited by guidelines. This study aimed to assess the efficacy of reported treatment options for patients with metastatic CC. **METHODS:** Searches of PubMed were conducted, with no date restrictions, to identify published randomised controlled Phase II/III clinical trials (RCTs) of chemotherapies recommended by treatment guidelines, and radiotherapy and/or surgery, that reported overall survival (OS) in patients with metastatic (systemic recurrent, persistent or *de novo*-metastatic) CC. Treatment guidelines and the Cochrane Library were also explored to identify additional citations. **RESULTS:** Of 65 articles identified, 10 articles published between 1987 and 2014 proceeded to data extraction. Evidence supporting the use of chemotherapy was limited to cisplatin-monotherapy or platinum-based combination therapy. Overall the OS benefit of these agents ranged from 0.9 to 2.9 months and 0.79 to 1.32 for hazard ratio (HR). The latest innovation, bevacizumab plus chemotherapy, demonstrated the greatest significant gain in OS versus chemotherapy (OS gain 3.7 months; HR 0.71; p=0.004). The study did not identify any RCTs that supported the use of surgery and/or radiotherapy in this setting; the evidence was limited to seven retrospective hospital based studies. **CONCLUSIONS:** This study highlighted an unmet need for additional treatment options for metastatic CC. Use of cisplatin-monotherapy or platinum-based combination therapy has provided limited survival benefits for many decades. The novel combination of bevacizumab plus chemotherapy has demonstrated an increase in survival in these patients. However, since there is no RCT evidence supporting the use of surgery and/or radiotherapy, a health technology appraisal of these alternative interventions is not currently feasible. Additional clinical research is urgently needed to assess the comparative clinical value of these therapies.

PCN12

COMPARISON OF MEAN OVERALL SURVIVAL (OS) AND RADIOGRAPHIC PROGRESSION FREE SURVIVAL (RPFS) BASED ON MATCHING ADJUSTED INDIRECT COMPARISON OF ABIRATERONE ACETATE AND ENZALUTAMIDE FOR THE TREATMENT OF CASTRATION-RESISTANT PROSTATE CANCER IN CHEMOTHERAPY NAÏVE PATIENTS

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OBJECTIVES: Abiraterone acetate plus predniso(lo)ne (AA) and enzalutamide (E) are novel therapies for the treatment of metastatic castration-resistant prostate cancer in chemotherapy naïve patients. Pivotal trials have been conducted evaluating the efficacy of the drugs using different comparators. In the COU-AA-302 trial, patients were randomised between AA and active comparator predniso(lo)ne whereas in the PREVAIL trial, E was compared against placebo. For health economic purposes, the mean overall survival (OS) and radiographic progression-free survival (rPFS) of both novel agents need to be compared in the absence of head-to-head trial data. **METHODS:** Due to the difference in the comparator arms, only survival data from AA and E were used for the comparison. Observed individual level survival data with baseline patient characteristics were available for AA. Individual survival data were simulated for E to replicate the rPFS and OS curves published for the pivotal trial. rPFS and OS were modeled and extrapolated by fitting parametric survival functions. The Weibull, exponential, and lognormal models were evaluated based on statistical and clinical considerations, i.e. assessing the model fit and the implied hazard profiles, respectively. To control for differences in baseline patient characteristics (PSA, ECOG, Gleason score, BPI, LDH, metastasis, age, race) rPFS and OS estimates for AA were adjusted using a matching algorithm. **RESULTS:** The Weibull models were selected for extrapolation of both OS and rPFS. The mean rPFS was estimated to be 23.9 (95% CI: 21.5-26.3) and 19.5 (95% CI: 16.0-23.9) months for AA and E respectively. Mean OS was estimated to be 38.7 (95% CI: 36.4-40.7) and 34.6 (95% CI: 31.8-37.8) months respectively. **CONCLUSIONS:** Based on currently available data and the presented modeling approach, these findings suggest that AA is associated with longer mean rPFS and OS than E.

PCN13

CLINICAL EFFECTIVENESS OF ROBOTIC IMAGE-GUIDED STEREOTACTIC RADIOSURGERY (CYBERKNIFE) IN SELECTED PRIMARY AND SECONDARY SOFT TISSUE NEOPLASMS: A SYSTEMATIC REVIEW

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OBJECTIVES: Effectiveness of radiosurgery for head and spinal neoplasms is established. The aim of this study was to systematically review the clinical literature of CyberKnife for people with selected primary and secondary soft tissue lesions. **METHODS:** A systematic search was conducted for best available clinical data for lung metastasis, primary and secondary liver cancer, locally advanced pancreatic cancer population treated with CyberKnife radiation. Searching using Medline, EMBASE, Cochrane Library took place in September 2013. **RESULTS:** Only one relevant comparative clinical study (matched-pair analysis) met the inclusion criteria, assessing effectiveness and safety of stereotactic radiosurgery and radiofrequency ablation for colorectal liver metastasis. For other neoplasms single-arm studies were found. Compared to RFA CyberKnife for liver metastasis was significantly better in median local disease free survival, which was 34.4 months vs. 6.0 months, (p<0.001). 1 and 2-year local control rates also favored CK (85.0% vs. 65.0% and 80.0% vs. 61.0%, respectively) but the difference wasn't significant. However, trend for better OS was found with RFA (34.4 vs. 52.3 months). For lung metastasis, treatment with CK resulted in 24.0-62.0% complete or partial response, 38.0-76.0% patients stabilized. In primary liver tumors OR (CR + PR) was observed in 63.0-86.0% patients, 0.0-29.0% stabilized, median PFS reached 10.0-15.8 months. Inconsistent results were seen in locally advanced pancreatic cancer population. In one study 92.0% responded or stabilized but in other only 1 patient of 77 had PR. Median OS was 6.4-10.3 months. All studies reported mostly mild adverse events after CK. Serious AE were rare. **CONCLUSIONS:** There is limited quality evidence on the effectiveness and safety of robotic image-guided stereotactic radiosurgery in patients with soft tissue neoplasms. Available studies are highly heterogenic in methods, patients characteristics and outcomes but suggest that CyberKnife may be beneficial in local tumor control. There is a need of well-designed comparative studies.

PCN14

ANALYSIS OF TREATMENT OPTIONS FOR RELAPSED OR REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

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OBJECTIVES: For patients with relapsed or refractory (R/R) chronic lymphocytic leukemia (CLL), treatment outcomes are poor and treatment options are limited. Ibrutinib is an oral, once-a-day, first-in-class covalent inhibitor of Bruton's tyrosine kinase approved by the Food and Drug Administration (FDA) for R/R CLL. In a recent phase III trial (PCYC-1112), ibrutinib was associated with improved progression-free survival (PFS, hazard ratio [HR] =0.215) and overall survival (OS, HR=0.387) versus ofatumumab. The aim of this study is to provide a summary and analysis of results observed with current therapies in high-risk patients with R/R CLL. **METHODS:** A systematic literature review and targeted literature search of clinical trials and international treatment guidelines in PubMed/MEDLINE (January 1,2001–April 28,2013) and ASCO/ASH/EHA conference proceedings (2011–2013) were conducted to identify and evaluate current treatment options for R/R CLL, including alemtuzumab, rituximab, bendamustine, chlorambucil, and ofatumumab. **RESULTS:** Study results highlight poor outcomes with existing treatment options and continuously high unmet need in patients. Sixteen trials were identified; the majorities were single-arm with small sample sizes, making comparative effectiveness difficult to establish. Time-to-treatment failure was 5.8 months with alemtuzumab, while median PFS was 5.5 months with rituximab, 5.5–5.7 months with ofatumumab, 8 months with chlorambucil-ritiximab, and 15.2 months in previously-treated patients and 6.8 months in previously-treated patients with del (17p) with bendamustine-rituximab. Ofatumumab has demonstrated activity in patients with difficult-to-treat, high-risk CLL and is the only recognized and approved treatment by health authorities globally in this treatment setting and recommended in treatment guidelines. **CONCLUSIONS:** The lack of standard of care creates challenges for defining comparators in clinical trials and health technology assessments. In R/R CLL with high-risk features, ofatumumab is an appropriate comparator. Interim results from the phase III RESONATE trial showed that ibrutinib achieved significantly improved efficacy versus ofatumumab, even in high-risk disease patients.

PCN15

AN INDIRECT TREATMENT COMPARISON OF CABOZANTINIB VERSE VANDETANIB IN PROGRESSIVE MEDULLARY THYROID CANCER (MTC)

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OBJECTIVES: MTC is a rare form of thyroid cancer with prevalence of less than 7 per 100,000. A majority of MTC patients have RET mutations, and RET M918T mutations are associated with especially poor prognosis. In 2012, EMA approved the first tyrosine kinase inhibitor (TKI) CAPRELSA® (vandetanib, VDB) for the treatment of MTC. In March 2014, the EMA approved another TKI -COMETRIQ® (cabozantinib, CBZ) for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC, with orphan drug status. The objective of this study was to assess the relative efficacy in PFS and OS of CBZ vs VDB. **METHODS:** Since there are no clinical trials directly comparing the two treatments, an adjusted indirect comparison (Bucher et al. method) was used. Evidence on PFS for the two treatments was collected from the pivotal clinical trials in MTC. The analysis considered all patients and a subgroup of RET M918T mutation positive (RET+) patients. Our analysis focused on PFS due to lack of evidence for the VDB OS in the RET M918T mutation subgroup. In the all patients analysis three different scenarios were explored: a logrank model to ensure comparability with the VDB data; a Cox model stratified on age at randomization and prior TKI status; and a Cox model without stratifications. **RESULTS:** In the subgroup analysis (logrank model) PFS was estimated to increase by 65% with CBZ comparing to VDB (HR 0.35; 95% CI 0.14-0.87). In the all-patients analysis the estimates were less conclusive: logrank model (HR 0.72; 0.40-1.28), Cox model with stratifications (HR 0.61; 0.35-1.04), Cox model without stratifications (HR 0.66; 0.39-1.13). **CONCLUSIONS:** The results showed a positive trend in favour of CBZ in PFS. Given the limited evidence a direct head-to-head comparison is necessary to validate the study findings.